



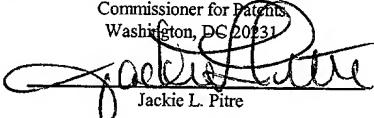
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Examiner: Unknown

Group/Art Unit: 1645

Atty. Dkt. No: 5119-00543

CERTIFICATE OF MAILING  
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 Commissioner for Patents  
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 Jackie L. Pitre

**BOX Amendment-No Fee**  
Commissioner for Patents  
Washington, D.C. 20231

Please amend the above-captioned application as follows:

Please amend the specification to read as follows. Applicant has submitted herewith a ~~striketrough~~ version of the specification.

Paragraphs beginning on page 186, line 24

FIGS 84 A-C depict alternate embodiments of masks having openings that produce projections after etching. As depicted in these figures different size shapes may produce different

Figure 1. The effect of the concentration of the *Agrobacterium* suspension on the transformation efficiency of *Agrobacterium* strains. The concentration of the *Agrobacterium* suspension was 10<sup>6</sup> cells/ml (a), 10<sup>7</sup> cells/ml (b), 10<sup>8</sup> cells/ml (c), 10<sup>9</sup> cells/ml (d), 10<sup>10</sup> cells/ml (e), and 10<sup>11</sup> cells/ml (f). The concentration of the *Agrobacterium* suspension was 10<sup>6</sup> cells/ml (a), 10<sup>7</sup> cells/ml (b), 10<sup>8</sup> cells/ml (c), 10<sup>9</sup> cells/ml (d), 10<sup>10</sup> cells/ml (e), and 10<sup>11</sup> cells/ml (f). The concentration of the *Agrobacterium* suspension was 10<sup>6</sup> cells/ml (a), 10<sup>7</sup> cells/ml (b), 10<sup>8</sup> cells/ml (c), 10<sup>9</sup> cells/ml (d), 10<sup>10</sup> cells/ml (e), and 10<sup>11</sup> cells/ml (f).

size cavities. As described in more detail below, the ability to form different size cavities and different having masks with different size openings may be useful for placing particles in the cavities. Any of the cavities formed with the above-described mask may be formed through substrate 1300 such that a bottom opening is also present.

An integrated cover layer of flexible projections 1340 formed in mask 1320 may provide a method of retaining particle 1350 in cavity 1330. In an embodiment shown in FIG. 85, flexible projections 1340 may be produced over cavity 1330. Mask opening 1310 may be smaller than the top of underlying cavity 1330. Particle 1350 may be inserted through flexible projections 1340 into cavity 1330 as depicted in FIG. 85. As particle 1350 passes flexible projections 1340, the flexible projections may elastically bend downward, as shown in FIG. 85B and FIG. 85C, until the particle passes completely by the flexible projections and into cavity 1330. As shown in FIG. 85D, after particle 1350 passes flexible projections 1340, the flexible projections may elastically return to their original position, thereby providing retention of the particle in cavity 1330. Retention of particle 1350 in cavity 1330 may be maintained by flexible projections 1340 during subsequent handling of the sensor array.

FIG. 86 shows cross sectional and top views of cavity 1330 with flexible projections 1340 formed for specific size selection of particle 1350 to be captured and retained in the cavity. In one embodiment, a  $100\text{ cm}^2$  silicon substrate may have from about  $10^1$  to about  $10^6$  mask openings and cavities. Mask openings 1310 may be substantially the same size across substrate 1300, or may be of different sizes. As shown in FIG. 86, the size and shape of top opening 1360 of cavity 1330 may be determined by location of corners 1380 of mask opening 1310. Size and shape of bottom opening 1370 may be determined by location of corners 1380 and thickness of substrate 1300. As such, the size and shape of the top and bottom openings for each cavity may be controlled independently. Each cavity 1330 and flexible projections 1340 may be designed for a specific size particle 1350.

An array of cavities 1330 in substrate 1300 may be formed to automatically sort specific size particles 1350 into specific cavities based on a size of the particle; e.g., based on the diameter of the particle. Large particle 1350 with a diameter larger than top opening 1360 of cavity 1330 may be substantially inhibited from entering the cavity. Large particle 1350 with a diameter smaller than bottom opening 1370 of cavity 1330 may enter top opening 1360 through flexible projections 1340. Smaller particle 1350 will then pass through bottom opening 1370 and out of the cavity. Small particle 1350 with a diameter smaller than top opening 1360 and larger than bottom opening 1370 may be captured in cavity 1330 and retained in the cavity with flexible projections 1340.

an embodiment of a sensor array, different sized particles 1350 may be used to target different types of analytes of interest. A mixture of particles having predetermined sizes may be introduced to the array. The array of cavities 1330 may be designed for specific particle sizes to automatically sort the correct size particle 1350 into each cavity. In a sensor array system, flexible projections 1340 may be transparent to the wavelength of light of a light source used for illuminating particles 1350 in cavities 1330.

Paragraph beginning on page 189, line 4.

In another embodiment, a cavity is formed in a substrate by undercutting a mask to produce flexible projections in the mask during anisotropic etching of a silicon substrate as described previously. The integrated cover layer formed by the mask and flexible projections and the top and bottom opening of the cavity in the substrate may be fabricated for a desired diameter size of a particle in a shrunken state. A particle to be placed within the cavity may be exposed to a medium in which the particle may be caused to shrink. As shown in FIG. 87A, particle 1350 may be easily inserted through flexible projections 1340 into cavity 1330 of substrate 1300 in its shrunken state. After insertion of particle 1350 into cavity 1330, the particle may be exposed to a medium, which causes the particle to return to its normal state as shown in

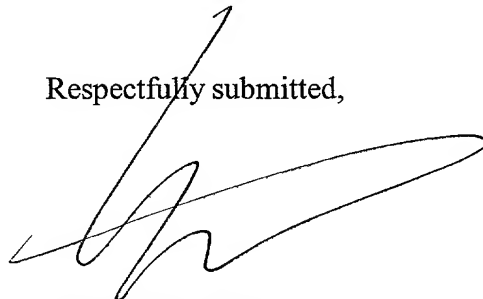
FIG. 87B. Particle 1350 may be captured within cavity 1330, by flexible projections 1340 after it returns to its normal size. By correctly designing the swollen state of particle 1350 and flexible projections 1340, the particle may be retained within the cavity during subsequent processing.

***In the Claims:***

Please cancel claims 1-308, 343-374, 376-398, 400-421 and 423-459 without prejudice.

It is believed that no fees are due in connection with the filing of this Preliminary Amendment. However, if any fees are due, the Commissioner is hereby authorized to deduct said fees from Conley, Rose & Tayon Deposit Account No. 50-1505/5119-00543/EBM.

Respectfully submitted,



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**Strike-through Version of Specification**

FIGS 84 A-C depict alternate embodiments of masks having openings that produce projections after etching. As depicted in these figures different size shapes may produce different size cavities. As described in more detail below, the ability to form different size cavities and different having masks with different size openings may be useful for placing particles in the cavities. Any of the cavities formed with the above described mask may be formed through substrate ~~Error! Reference source not found.~~ 1300 such that a bottom opening is also present.

An integrated cover layer of flexible projections 1340 formed in mask ~~1320~~ 1320 may provide a method of retaining particle 1350 in cavity ~~1330~~ ~~Error! Reference source not found.~~

In an embodiment shown in FIG. 85, flexible projections 1340 may be produced over cavity 1330. Mask opening ~~1310~~ 1310 may be smaller than the top of underlying cavity ~~Error!~~ ~~Reference source not found.~~ 1330. Particle 1350 may be inserted through flexible projections 1340 into cavity ~~Error! Reference source not found.~~ 1330 as depicted in FIG. 85. As particle 1350 passes flexible projections 1340, the flexible projections may elastically bend downward, as shown in FIG. 85B and FIG. 85C, until the particle passes completely by the flexible projections and into cavity ~~Error! Reference source not found.~~ 1330. As shown in FIG. 85D, after particle 1350 passes flexible projections 1340, the flexible projections may elastically return to their original position, thereby providing retention of the particle in cavity ~~Error! Reference source not found.~~ 1330. Retention of particle 1350 in cavity ~~Error! Reference source not found.~~ 1330 may be maintained by flexible projections 1340 during subsequent handling of the sensor array.

FIG. 86 shows cross sectional and top views of cavity ~~Error! Reference source not found.~~ 1330 with flexible projections 1340 formed for specific size selection of particle 1350 to be captured and retained in the cavity. In one embodiment, a 100 cm<sup>2</sup> silicon substrate may have from about 10<sup>1</sup> to about 10<sup>6</sup> mask openings and cavities. Mask openings ~~1310~~ 1310 may be substantially the same size across substrate ~~Error! Reference source not found.~~ 1300, or may be

of different sizes. As shown in FIG. 86, the size and shape of top opening 1360 of cavity ~~Error! Reference source not found.~~ 1330 may be determined by location of corners 1380 of mask opening 1310 ~~in mask 1320~~. Size and shape of bottom opening 1370 may be determined by location of corners 1380 and thickness of substrate ~~Error! Reference source not found.~~ 1300. As such, the size and shape of the top and bottom openings for each cavity may be controlled independently. Each cavity ~~Error! Reference source not found.~~ 1300 and flexible projections 1340 may be designed for a specific size particle 1350.

An array of cavities ~~Error! Reference source not found.~~ 1330 in substrate ~~Error! Reference source not found.~~ 1300 may be formed to automatically sort specific size particles 1350 into specific cavities based on a size of the particle; e.g., based on the diameter of the particle. Large particle 1350 with a diameter larger than top opening 1360 of cavity ~~Error! Reference source not found.~~ 1330 may be substantially inhibited from entering the cavity. Large particle 1350 with a diameter smaller than bottom opening 1370 of cavity ~~Error! Reference source not found.~~ 1330 may enter top opening 1360 through flexible projections 1340. Smaller particle 1350 will then pass through bottom opening 1370 and out of the cavity. Small particle 1350 with a diameter smaller than top opening 1360 and larger than bottom opening 1370 may be captured in cavity ~~Error! Reference source not found.~~ 1330 and retained in the cavity with flexible projections 1340.

In an embodiment of a sensor array, different sized particles 1350 may be used to target different types of analytes of interest. A mixture of particles having predetermined sizes may be introduced to the array. The array of cavities ~~Error! Reference source not found.~~ 1330 may be designed for specific particle sizes to automatically sort the correct size particle 1350 into each cavity. In a sensor array system, flexible projections 1340 may be transparent to the wavelength of light of a light source used for illuminating particles 1350 in cavities ~~Error! Reference source not found.~~ 1330.

In another embodiment, a cavity is formed in a substrate by undercutting a mask to produce flexible projections in the mask during anisotropic etching of a silicon substrate as described previously. The integrated cover layer formed by the mask and flexible projections and the top and bottom opening of the cavity in the substrate may be fabricated for a desired diameter size of a particle in a shrunken state. A particle to be placed within the cavity may be exposed to a medium in which the particle may be caused to shrink. As shown in FIG. 87A, particle 1350 may be easily inserted through flexible projections 1340 into cavity ~~Error!~~ ~~Reference source not found.~~ 1330 of substrate ~~Error!~~ ~~Reference source not found.~~ 1300 in its shrunken state. After insertion of particle 1350 into cavity ~~Error!~~ ~~Reference source not found.~~ 1330 the particle may be exposed to a medium, which causes the particle to return to its normal state as shown in FIG. 87B. Particle 1350 may be captured within cavity ~~Error!~~ ~~Reference source not found.~~ 1330 by flexible projections 1340 after it returns to its normal size. By correctly designing the swollen state of particle 1350 and flexible projections 1340, the particle may be retained within the cavity during subsequent processing.